

## AMENDMENTS TO THE CLAIMS

Applicant respectfully requests that claims 24-28, 32-35, 37-44, 55-57 and 59-72 be canceled, and that new claims 81-103 be added.

Claims 1-80 (canceled).

Claim 81 (new): A method of screening for hereditary colorectal cancer or a predisposition to hereditary colorectal cancer in an organism, said screening method comprising:

- (a) isolating a biological sample containing normal cells from said organism;
- (b) preparing a lysate of said normal cells;
- (c) preparing a protein extract from said lysate of said normal cells;
- (d) immunologically quantitating the levels of two or more wild-type subject proteins in said protein extract of said normal cells, wherein said subject proteins are selected from the group consisting of MLH1, MSH2, MSH6, PMS1, PMS2, and APC proteins;
- (e) calculating the ratio of the level of one wild-type subject protein in said normal cells, to the level of one or more of the other wild-type subject proteins in said normal cells; and

(f) determining whether the ratio or ratios calculated in step (e) reflects or reflect an about 50% decrease in the normal level of any of the subject proteins for which a wild-type level was immunologically quantitated;

(g) whereby if the ratio or ratios calculated in step (e) indicates or indicate that there is an about 50% decrease in the normal level of one of the wild-type subject proteins in said normal cells, that the subject organism has hereditary colorectal cancer or has a predisposition to hereditary colorectal cancer.

Claim 82 (new): The method of Claim 81 wherein step (f) comprises comparing the ratio or ratios calculated in step (e) to a comparable mean or means of ratios calculated from the levels of wild-type subject proteins in comparable biological samples from organisms of the same taxonomic classification as the subject organism, wherein said organisms of the same taxonomic classification as the subject organism are unaffected by said hereditary colorectal cancer or predisposition to hereditary colorectal cancer.

Claim 83 (new): The method of Claim 81 wherein said organism is a vertebrate.

Claim 84 (new): The method of Claim 83 wherein said vertebrate is a mammal.

Claim 85 (new): The method of Claim 84 wherein said mammal is a human.

Claim 86 (new): The method of Claim 81 wherein said biological sample is selected from the group consisting of body fluids and tissue specimens.

Claim 87 (new): The method of Claim 86 wherein said body fluids are selected from the group consisting of blood, serum, plasma, semen, breast exudate, gastric secretions, fecal suspensions, bile, saliva, tears, sputum, mucous, urine, lymph, cytosols, ascites, pleural effusions, amniotic fluid, bladder washes, bronchoalveolar lavages, and cerebrospinal fluid.

Claim 88 (new): The method of Claim 81 wherein said normal cells are peripheral blood lymphocytes.

Claim 89 (new): The method of Claim 81 wherein said method is diagnostic or diagnostic/prognostic for hereditary colorectal cancer or a predisposition to hereditary colorectal cancer.

Claim 90 (new): The method of Claim 81 wherein said hereditary colorectal cancer is selected from the group consisting of hereditary non-polyposis colon cancer (HNPCC) and familial adenomatous polyposis (FAP).

Claim 91 (new): The method of Claim 81 wherein the subject proteins are mismatch repair proteins.

Claim 92 (new): The method of Claim 91 wherein the subject proteins are selected from the group consisting of the MLH1, MSH2, MSH6, PMS1, and PMS2 proteins; and said hereditary colorectal cancer is or said predisposition to hereditary colorectal cancer is for hereditary non-polyposis colon cancer.

Claim 93 (new): The method of Claim 92 wherein the subject proteins are the MLH1 protein and the MSH2 protein.

Claim 94 (new): The method of Claim 81 wherein the level of each wild-type subject protein is determined by Western blot analysis, by immunoprecipitation and then by Western blot analysis, by flow cytometry, by EIA, by ELISA, by RIA, by competition immunoassay, by dual antibody sandwich assay, by chemiluminescent assay, by bioluminescent assay, by fluorescent assay, or by agglutination assay.

Claim 95 (new): The method of Claim 81 which is automated.

Claim 96 (new): The method according to Claim 82 wherein the ratio or ratios calculated in step (e) when compared to said mean or means of ratios indicates that the about 50% decrease in the normal level of one of the wild-type subject proteins in said sample is about  $50\% \pm 20\%$  of the level of said one wild-type subject protein in

comparable samples from organisms unaffected by said hereditary colorectal cancer or predisposition to hereditary colorectal cancer.

Claim 97 (new): The method according to Claim 82 wherein the ratio or ratios calculated in step (e) when compared to said mean or means of ratios indicates that the about 50% decrease in the normal level of one of the wild-type subject proteins in said sample is about  $50\% \pm 15\%$  of the level of said one wild-type subject protein in comparable samples from organisms unaffected by said hereditary colorectal cancer or predisposition to hereditary colorectal cancer.

Claim 98 (new): The method according to Claim 82 wherein the ratio or ratios calculated in step (e) when compared to said mean or means of ratios indicates that the about 50% decrease in the normal level of one of the wild-type subject proteins in said sample is about  $50\% \pm 10\%$  of the level of said one wild-type subject protein in comparable samples from organisms unaffected by said hereditary colorectal cancer or predisposition to hereditary colorectal cancer.

Claim 99 (new): The method of Claim 91 wherein the normal biological sample comprises peripheral blood lymphocytes.

Claim 100 (new): The method of Claim 93 wherein the normal biological sample comprises peripheral blood lymphocytes.

Claim 101 (new): The method of Claim 81 wherein an about 50% decrease in the normal level of wild-type APC protein is indicated, and that result indicates that the organism has familial adenomatous polyposis (FAP) or a predisposition to FAP.

Claim 102 (new): The method of Claim 81 wherein said about 50% decrease in the normal level of one of the wild-type subject proteins is the result of a germline mutation selected from the group consisting of nonsense mutations, frameshift mutations, promoter mutations, enhancer mutations, splice site mutations, null mutations, and poly-A tail mutations.

Claim 103 (new): The method of Claim 81 wherein said about 50% decrease in the normal level of one of the wild-type subject proteins is the result of a germline mutation selected from the group consisting of truncation-causing mutations and mutations that cause allelic loss.